

# EXHIBIT A

IN THE UNITED STATES DISTRICT COURT  
FOR THE NORTHERN DISTRICT OF ILLINOIS  
EASTERN DIVISION

PSN ILLINOIS, LLC, )  
an Illinois corporation, )  
Plaintiff, ) Case No.  
vs. )  
Sigma-Aldrich Corp., EMD Biosciences )  
Inc., VWR International LLC, Orbigen, )  
Inc., Axxora Life Sciences, Inc., )  
Cayman Chemical Company, Inc., )  
Origene Technologies, Inc., Superarray )  
Bioscience Corp., Tocris Bioscience, and )  
Millipore Corp. ) COMPLAINT FOR  
Defendants. ) PATENT INFRINGEMENT  
FILED: JULY 1, 2008  
08CV3742  
JUDGE PALLMEYER  
MAGISTRATE JUDGE VALDEZ  
TG  
DEMAND FOR JURY TRIAL

**COMPLAINT**

1. Plaintiff, PSN ILLINOIS, LLC. ("PSN"), complains of defendants ("Defendants") as follows:

**NATURE OF LAWSUIT**

2. This is a claim for patent infringement arising under the patent laws of the United States, Title 35 of the United States Code.

**THE PARTIES**

3. PSN is an Illinois corporation with a place of business at 280 W. Adams Street, Chicago, Illinois 60604. PSN is the assignee of, and owns all rights, title and interest in and to, and has standing to sue for past, present and future infringement of: United States Patent No. 5,856,443, entitled "Molecular Cloning And Expression of G-Protein Coupled Receptors," issued on Jan. 5, 1999 ("the '443 patent") (Exhibit A); and

United States Patent No. 6,518,414B1, entitled "Molecular Cloning And Expression of G-Protein Coupled Receptors," issued on Feb. 11, 2003 ("the '414 patent") (Exhibit B) (collectively "PSN's Patents").

4. Defendant Sigma-Aldrich Corp. (Sigma) is a company incorporated in Delaware with a principal place of business at 3050 Spruce Street, St. Louis, MO 63103. Sigma transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

5. Defendant EMD Biosciences Inc. (EMD) is a company incorporated in New York with principal places of business at 10394 Pacific Center Court, San Diego, CA 92121, 441 Charmany Drive, Madison, WI 53719, and 480 S. Democrat Road, Gibbstown, NJ 08027. EMD transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

6. Defendant VWR International LLC (VWR) is a company incorporated in Delaware with its principal place of business at 1310 Goshen Parkway, West Chester, PA 193850. VWR transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

7. Defendant, Orbigen, Inc. (Orbigen) is a company incorporated in California with its principal place of business at 6827 Nancy Ridge Drive, San Diego, CA 92121. Orbigen transacts business and has sold to customers and/or offered for sale, in

this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

8. Defendant, Axxora Life Sciences, Inc. (Axxora) is a company incorporated in Delaware with its principal place of business at 6181 Cornerstone Court East, Suite 103, San Diego, CA 92121. Axxora transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

9. Defendant, Cayman Chemical Company Inc. (Cayman) is a company incorporated in Colorado with its principal place of business at 1180 E. Ellsworth Rd., Ann Arbor, MI 48108. Cayman transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

10. Defendant, Origene Technologies, Inc. (Origene) is a company incorporated in Delaware with its principal place of business at 6 Taft Court, Suite 300, Rockville, MD 20850. Origene transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

11. Defendant, Superarray Bioscience Corporation (Superarray) is a company incorporated in Delaware with its principal place of business at 15 Wormans Mill Court, Suite 101, Frederick MD 21701. Superarray transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

12. Defendant, Tocris Bioscience (Tocris) is a company incorporated in Delaware with its principal place of business at 16144 Westwoods Business Park, Ellisville, MO 63021. Tocris transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

13. Defendant, Millipore Corporation (Millipore) is a company incorporated in Massachusetts with its principal place of business at 290 Concord Rd. Billerica, MA 01821. Millipore transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

**JURISDICTION AND VENUE**

14. This Court has exclusive jurisdiction over the subject matter of the Complaint under 28 U.S.C. §§ 1331 and 1338(a).

15. Venue in this judicial district is proper under 28 U.S.C. §§ 1391(b), (c), (d) and/or 1400(b).

**THE DEFENDANTS' ACTS OF PATENT INFRINGEMENT**

16. Defendant Sigma has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following products:

- i. S1P2 C-Terminal Blocking Peptide (Catalog # E8028);

ii. Anti-S1P2, C-Terminal antibody produced in rabbit (Catalog # E7278);

iii. Monoclonal Anti-S1P2, C-Terminal antibody produced in mouse (Catalog # E4767); and

iv. Monoclonal Anti-S1P2, N-Terminal antibody produced in mouse (Catalog # E4892).

17. Defendant EMD has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following: Anti- EDG 5 (Ab-1) Mouse mAb (Catalog # GR44).

18. Defendant VWR has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following: S1P2 Receptor Antagonist (Catalog # 80017-352).

19. Defendant Orbigen has infringed claims of at least the '443 and '414 patents through, among other activities, the manufacture, use, offer for sale, sale, and/or distribution of products and service utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including these products:

i. Rabbit Endothelial differentiation sphingolipid G-protein-coupled receptor 5 (EDG5) polyclonal antibody (Catalog # PAB-10630); and

ii. Chicken Endothelial differentiation sphingolipid G-protein-coupled receptor 5 (EDG5) polyclonal antibody (Catalog # PAB-U0005).

20. Defendant Cayman has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and service utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following: JTE-013 (Catalog # 10009458).

21. Defendant Axxora has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and service utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including at least the following product corresponding to Cayman catalog: JTE-013 (Catalog # CAY-1009458).

22. Defendant Origene has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including these products:

i. Homo sapiens endothelial differentiation, sphingolipid G-protein coupled receptor, 5 (EDG5) as 10ug transfection ready DNA NM\_004230.2 (Catalog # SC117485);

ii. HuSH 29mer shRNA Constructs against EDG5 Locus ID = 9294 (Catalog # TR313297);

- iii. ORF Clone of Homo sapiens endothelial differentiation, sphingolipid G-protein-coupled receptor, 5 (EDG5) as 10 ug transfection ready DNA NM\_004230.2 (Catalog # RC210163); and
- iv. shRNA constructs against Mus musculus Edg5 Locus ID = 14739 (Catalog # TR513284).

23. Defendant Superarray has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including these products:

- i. Human G-Protein-Coupled Receptor Signaling PathwayFinder™ (Catalog # PAHS-071);
- ii. RT<sup>2</sup> PCR Primer Set for Mouse EDG 5: Endothelial differentiation, sphingolipid G-protein coupled receptor, 5 (Catalog # PPM05309A);
- iii. Oligo GE Array Human G-Protein-Coupled Receptor Signaling PathwayFinder™ (Catalog # OHS-071 and EHS-071); and
- iv. SureSilencing shRNA Plasmid for Human EDG5: Endothelial differentiation, sphingolipid G-protein coupled receptor, 5 (Catalog # KHO2350G for the GFP marker or KH02350N for the Neomycin resistance marker).

24. Defendant Tocris has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of

products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  (“S1P2”) that fall within the scope of claims of these patents, including at least the following product: S1P receptor antagonist, highly selective for S1P2 (EDG-5) (Catalog # 2392 JTE-013).#

25. Defendant Millipore has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  (“S1P2”) that fall within the scope of claims of these patents, including these products and services:

- i. EDG5 AdenoSilence<sup>TM</sup> RNAi Virus Human (Catalog # GAL 10065-V7);
- ii. EDG5 AdenoSilence<sup>TM</sup> RNAi Virus Human (Catalog # GAL 10065-V6);
- iii. EDG5 AdenoSilence<sup>TM</sup> RNAi Virus Human (Catalog # GAL 10065-V5);
- iv. EDG5 AdenoSilence<sup>TM</sup> RNAi Kit Human (Catalog # GAL 10065);
- v. ChemiSCREEN<sup>TM</sup> S1P2 Calcium-Optimized FLIPR Cell Lines (Catalog # HTS078C);
- vi. ChemiSCREEN<sup>TM</sup> Human Recombinant S1P2 Lysophospholipid Receptor Calcium Optimized Ready to Assay<sup>TM</sup> (Catalog # HTS078F);
- vii. ChemiSCREEN<sup>TM</sup> Human Recombinant S1P2 Lysophospholipid Receptor Membrane Preparation (Catalog # HTS0078M); and

viii. GPCRProfiler Services which screens compounds on receptors including the S1P2 receptor.

26. The defendants' infringement, contributory infringement and inducement to infringe have injured and will continue to injure PSN unless and until this Court enters an injunction prohibiting further infringement and, specifically, enjoining further manufacture, use, offer for sale, sale and/or distribution of products and/or processes that fall within the scope of PSN's Patents.

**PRAYER FOR RELIEF**

WHEREFORE, PSN asks this Court to enter judgment against the defendants, and against their subsidiaries, affiliates, agents, servants, employees and all persons in active concert or participation with them, granting the following relief:

- A. An award of damages adequate to compensate PSN for the infringement of PSN's Patents that has occurred, together with prejudgment interest.
- B. Increased damages as permitted under 35 U.S.C. § 284.
- C. A finding that the case is exceptional and an award to PSN of its attorney fees and costs as provided by 35 U.S.C. § 285.
- D. A permanent injunction prohibiting further infringement, inducement and contributory infringement of PSN's Patents.
- E. Such other and further relief as this Court or a jury may deem proper and just.

**JURY DEMAND**

PSN demands a trial by jury on all issues presented in this Complaint.

FOR PSN ILLINOIS, LLC

/s/ Michael P. Mazza

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JUDGE PALLMEYER

MAGISTRATE JUDGE VALDEZ

TG

## EXHIBIT A



US005856443A

# United States Patent [19]

MacLennan

[11] Patent Number: 5,856,443  
 [45] Date of Patent: \*Jan. 5, 1999

[54] MOLECULAR CLONING AND EXPRESSION OF G-PROTEIN COUPLED RECEPTORS

[76] Inventor: Alexander John MacLennan, 7811 NW. 35th Pl., Gainesville, Fla. 32606

[\*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 5,585,476.

[21] Appl. No.: 760,936

[22] Filed: Dec. 6, 1996

#### Related U.S. Application Data

[63] Continuation of Ser. No. 196,989, Feb. 15, 1994, Pat. No. 5,585,476.

[51] Int. Cl. 6 C07K 14/705; C12N 15/12

[52] U.S. Cl. 530/350; 435/69.1; 435/252.3; 435/320.1; 536/23.5

[58] Field of Search 435/69.1, 252.3, 435/320.1; 530/350; 536/23.5

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Primary Examiner—John Ulm

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[57] ABSTRACT

The cloning and expression of two novel rat cDNAs ("H218" and "rat-edg") which encode two members ("p<sup>H218</sup>" and "p<sup>rat-edg</sup>") of the G-protein coupled receptor superfamily of proteins is described. The amino acid sequence similarity between "p<sup>H218</sup>" and "p<sup>rat-edg</sup>" suggests that they may be activated by the same endogenous ligand (s). The expression pattern of mRNA transcripts of both genes in cell lines, various rat tissues and developing rat brain suggests that they both play a role in cell proliferation and/or differentiation. The polynucleotide molecules, proteins, and antibodies of the subject invention can be used in both diagnostic and therapeutic applications.

5 Claims, 12 Drawing Sheets

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-UCCCCCCCCCTCGAGCACAGCCAAACAGTCACCAAAAGTCAGCCACTGGCTGTCCCCGG  
 GGCGAGACGCCAAGGCCACTCGGCCGGGGAGGGACCCCTGGGGGGCTAGCCAGTGCT  
 CAGTCCCCATGGCCCCGGCCACTGAGCCCACCATCGGGTTATACTCAGAGTAC 8  
 MetGlyGlyLeutyrSergluty 8  
  
 25 CTCATACTCTGAGAAGGTTCAAGAACACTACATTACACCAAGGAGACCCGGACATGCAG  
 LeuAsnProGluLysvalGlnGluHistYrsntyrThrLysgluthrLeuAspMetGln 28  
  
 85 GAGACGCCCTCCCGGAAAGGTGGCCTCCGCCCTCATCATCATATTATGCTGTGCCATCGTG  
 GluthrProSerArgLysvalAlaSerAlaPheIleIleLeuCysysAlaIleVal 48  
  
 145 GTGGAGAACCTCTGGTGCTAATGCAGTGGCCAGGAACACGAAAGTTCACACTCAGGCCATG  
 ValGluAsnLeuLeuValleIleAlavalAlaArgAsnSerLysPheHisSerAlaMet 68  
  
 205 TACCTGTTCTCGCCAACCTGCCAGCGACCTCCGACTCTGGCAGGGCTGGCTGGCTTCCGGCC  
 TyrLeuPheIleGlyAsnLeuAlaAlaSerAspLeuAlaGlyValAlaPheValAla 88  
  
 265 AACACCTTGCTCTCCGGACACTGTACCCCTGTCCTTAACTCCCTTGCAAGTGGTTGCCCGA  
 AsnThrLeuSerGlyProValThrLeuSerLeuThrProLeuGlnTrpPheAlaArg 108  
  
 325 GAGGGTTCAAGCCTCATCACGCTCTGGCTCGGGTCTAGGCCATTGCCATC  
 GluglySerAlaPheIleIleLeuSerAlaSerValPheSerLeuLeuAlaIleAlaIle 128  
  
 385 GAGAGACAAAGTGGCCATGCCAAGGTCAAGCTCTAGGCCAGTGACAAAGCTGTGCAATG  
 GluArgGlnValAlaIleAlaIysVallySleutyrGlySerAspLysSerCysArgMet 148  
  
 445 TTGATCCTCATGGGGCCTCTGGCTGATATCGCTGATTCTGGCTGGCTTGCCCATCCTG  
 LeuMetLeuIleGlyAlaSerIrpLeuIleSerLeuIleLeuGlyGlyLeuProIleLeu 168  
  
 505 GGCTGGAAATTGTCGACCATCTGGAGGCCCTGCTCCTACTGTGGCTGCCCCCTCTATGCTAAG  
 GlyTrpAsnCysLeuAspHisIleGluAlaCysSerThrValLeuProLeutyrAlaLys 188  
  
 565 CACTATGTCCTCTGGCTCACCATCTCTCTGCTCATCTGGCTATCGTGGCCCTTG  
 HistYrvallLeuCysvalValThrIlePheSerValIleLeuAlaIleValAlaLeu 208

FIG. 1A

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625	TACGGTCCGAATCTACTTCGTTAGTCCGCTCAAGGCCATGCGGACGGTTCGCTGGCTCAGACG TyrValArgIleTyrPheValValArgSerSerHisAlaAspValAlaGlyProGlnThr	228
685	CTGGCCCTGCTCAAGACAGTCACCATCGTACTGGTGTTCATCATCTGCTGGCTGCCG LeuAlaLeuLeuLeuIleUlysthrValThrIleValLeuGlyValPheIleCysTrpLeuPro	248
745	GCTTTAGGCATCCTTCTCTAGACTCTACCTGTCCCGTCCGGCCTGTCCCTGTCTACTAC AlaPheSerIleLeuLeuAspSerThrCysProValArgAlaCysProValLeuTyr	268
805	AAAGCCCCATTATTCTTTGCCCTGCCACCCCTCAACTCTCTGCTCAACCCTGTCATCTAT LysAlaHistYrPhePheAlaPheAlaThrLeuAsnSerLeuLeuAsnProValIleTyr	288
865	ACATGGCGTAGCCGGACCTTCGGAGGGAGGTACTGAGGGCCCTGCTGTCGCTGGGGCAG ThrTrpArgSerArgAspLeuArgArgGluValLeuArgProLeuLeuCysTrpArgGln	308
925	GGAAAGGGGCAACAGGGCCAGAGGGTGGTCAACCGACTCCTGCCCTCCGC GlyLysGlyAlaIleGlyArgGlyArgArgIleLeuProLeuProLeuArg	328
985	AGCTCCAGCTCCCTGGAGAGGGCTTGCATATGCCATACATGCCAACATTCTGGAGGGC SerSerSerSerLeuGluArgGlyLeuHisMetProThrSerProThrPheLeuGluGly	348
1045	AACACACTGTCTGAGGGAAATGTGAACTGATCTGTAACCAAGCCACAGAGAGCTCT AspThrValVal	352

FIG. 1B

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1105 GTGGGAGGACCCAGGTGACCTCATCATGTCCCCCATGGTCCACAGGCTCTGGAGGAACTGA  
 1165 CCACGGCTCATAGGTCAAGGTGCCAACGGAGGGCAACTGACTAATCAGATTAGTACTGTG  
 1225 ACTGTGGGACCAATTAGGGTCTAGGGGACAGGAGGGCTCGAGTTAGGGCTAGACATT  
 1285 GCCACTTGGTACATGGGTGTCGGCATCCTGTCCTATCTCCAGCTTCCGGGTTCC  
 1345 CTTCCCTGCCTCCTCCTTAAGGGCTCTACATAGCCCCGGCTGGCTAGAGCTTGCTG  
 1405 TGCAGACCCAGGCTGACCTGGACCTCCAGAGATAAGATAACTGTCCTGAGTGCT  
 1465 GGGATTAAAGCCGTGTGCCACCCGGCTCCTGCCACCTTCCAGAAGCAATCTTA  
 1525 GGCCACACTTGGTTGAGGAACACTCTCCCAAGGGACCCAAAGCCTTCCCTGTCTCTG  
 1585 AGGCCCTGAATTCACAGCTTCCCAATTATCAACTGCTGCTTCCCTTCCCTGTG  
 1645 TTCAAGGGAAACCAACTGTGGGGCAGGGAGGGTCCCTGGGATCCCAAGTTATGCTCAG  
 1605 ATCTCACTGAGCACTTGGCTTATTGGGAGGAGAGAGGAATCAGCTGAGGCAGTGGGG  
 1665 CAGATGTTGAGGAAATTGGCTTCCTGGTGAAGAAACTCTAGGGAGGGCTTGGTTAT  
 1725 TCCTGGAACCCAGCCTCTTCCCAACGAACACTCTTCACACCCGAGCCTGAGCTGGATGC  
 1785 AAAGGCTGCTTCAAATTGTCTTTGTAGTTTGTGTTTTGTTTTAAATT  
 1845 GGGACAGGATCTCACGTACCCAGGCTCCGACTCACTATGTAGCCAAGGGCTGGCT  
 1905 TTGGACTTCTGACCCCTCTGCCCTCCGGCTCTGGAGTGCAAGGTATTACAAGGGTACAC  
 1965 CACCAACCACCAACAAACAACAAACACACCCAGGCTCCGACTTGTGAAACTATCATGA  
 2025 ATGACATGGTTACATAGCCTTGGTGGCCAAGGGACATCCGGATACTCTTATGGCATCT  
 2085 TCCTTGAAGGACTTGTGCTGCTGTAATCCTGTGGAGAGTAGAAATCCAAATACGGTACAAACGG  
 2145 TATTIAGTGTGTCTGTGTATCAGTGTGGGTCTGTGACCTCCTATCCAGTGTGGGTGC  
 2205 TGTCGTACCTCTATGTGCACATCCGTGTCAAGACTGCTAGAGAGATGGACGGGGTGTG  
 2265 TGTCCTTGTTGGGTCTAGCCATGATCAGGGCTCCTGGGAATTGCTGAATCATCTCC  
 2325 ACACACAGACACACCCCTCCGGCTTAAGAAATGTGTGAAAGAAAGGCTGAGGAAGGG  
 2385 AGATTGGAGGCAAGGAGCCAGTCGGAGTGTCTCCCTCATACAGCTTCCAGATG  
 2445 TCCCCCTTGTGCTGAAACCCAGAACTGGCCATAAAACAGTCAATTCTCAATT  
 2505 AAA

FIG. 1C

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FIG. 2A

**TMD#2**

SAMVNTLISCPVTISLT  
TINYL. IVSLAVADLLVATLYMPVTVYLEVCEWKFS...  
VTINY. EITSLACADLVMGLAVVPTFISHIMKMMNGF...  
PON. LEIVSLASADLIVATVLTPELANEVGMGYWFG...  
VANYL. IGSIAVTDMEYSVLVEMLIYQVINKWTG...  
VNNY. EILSLACADLILSTSMLNLYTTLGMGHWAIG...  
VTINY. EIVNLALADLCHAFAFNAAENVYASHNIWYFG...  
[REDACTED]

TMD#4  
 TMD#3  
 3218 PLOWPAREGS AFITIS . ASVFSLLAIAERQVATAKVQLYGSDKS . CRMMLIGASWMLISLICGCLPIL . GM  
 2 . RIH . CDIFVFTLDYMMCTASILNLCAISIDRYTAVAMPMLNTRYSSKRVYTMIAWVULSFTISC . PLIFGLI  
 2 . NFW . CEFWTSIDWICVCTASIEITLCAIVDRYIAITSPFKYQSSLITKNCAR . WVILMWMIVSGLTSFLPIOMHM  
 2 . KDN . CEIYIALLDVFCTSSIVHLCAILSDRYWSITOAIEN . LKRTPRRIKAIITTVWVISAVISSEPPLISIE  
 HTIA . QVT . CDLFIJALDVLCCCTSIIHLCAIALLDRIWAITDPIDVNKRTPRRAFT . SIT . WLIGFLISIPPMTGWR  
 1 . TLA . CDLWMLADYVANASVMMNLISEDRYFSVTRPLSMRAKTPRRAALM . IGLAMLVSFWA . PAIIFW  
 .RAF . CYFQNLFPITAMFVSIYSMTIAIDRYMAIVHPPQRL . SAPGTR . AV . IAGIIVLVALALAF . BOCEYSS  
 K

TMD#5  
CLIDHLEACST...VLPLYAKHYVLCVTFSVILLA  
NTDQNE.....CLIANPAFVYVSSVSFVVPF  
RATHOKA...IDCYHRETCCDFFTNQAYAIISSAIVSF  
KGGGGGGPQ...PAEPRCEINDQKWWYUSSCGSF  
PEDRSDPDA.....CTISKDMGTYIYSTFCGF  
YLVEG...RTYLAGQCYTOFLSQPILIEGTGTAAMAF  
ITTDEGAIIKCVVAWPEDSGKMLLYHLIVIALITYF

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**FIG. 2B**

TMD#6  
 P<sup>F218</sup>  
 D2 LIVVYKIVIYLKRKRVRNTK- (112) -KEKKATQMLIAIVLGVFICWLPPFITHILNIHC...DCNI.P  
 β2 LVMMVFVYSRVFQVAKRQLOK- (33) --KEHKALKTGLIIMGIFTLICWLPPFIVNIVHVI...QDNLI.P  
 α2 CLIMILVYVRIYQIAKRRTRV- (138) -REKRFTFVLAIVVGFVFVWCWFPEFFTYTITAV...GCSV.P  
 5HT1A LILMLVYGRIFRAARFRIPK- (111) -RERKTVKTLGIMGTFILICWLBEFIVALVLPFCE..SSCHM.P  
 M1 VTMCTLYWRIYRETNARE- (138) -KEKKAARTLSSAIIILAFIVTWTIPYNIMMVLVSTFC..KDC.V.P  
 SK LVMMFVAYSVIGLTLWRRSVP- (13) --AKKKFVKTMVLYVVTFAICWLPPYHLYFILGTFQEDIYCHKFI

KAHY. . FFAFATLNSLNPVIYTWRSDLRREVLRPILC--(46)  
PVLYSAFTWLGYVNSAVNPIIYTTFNIEFRKAFMKILHC  
KEVYILLNLWLGYVNSAFNPLIYC. RSPDFERIAFQELL. C--(37)  
RTLFKFEEWFGYCNSSLNPVITYTIFNHDFRAFKKIL. C--(8)  
TLLGATINWLGYNSNSLNPVITYAYFNKDFQNAFKKIIKC--(5)  
ETLWELGYWLGYNSTINPMCYALCNKAFRDTFRLLILC--(2.5)  
QOYVLLAELWLAMSTMYNPIIYCCLNHRFRSGFRLAFRC--(6.3)

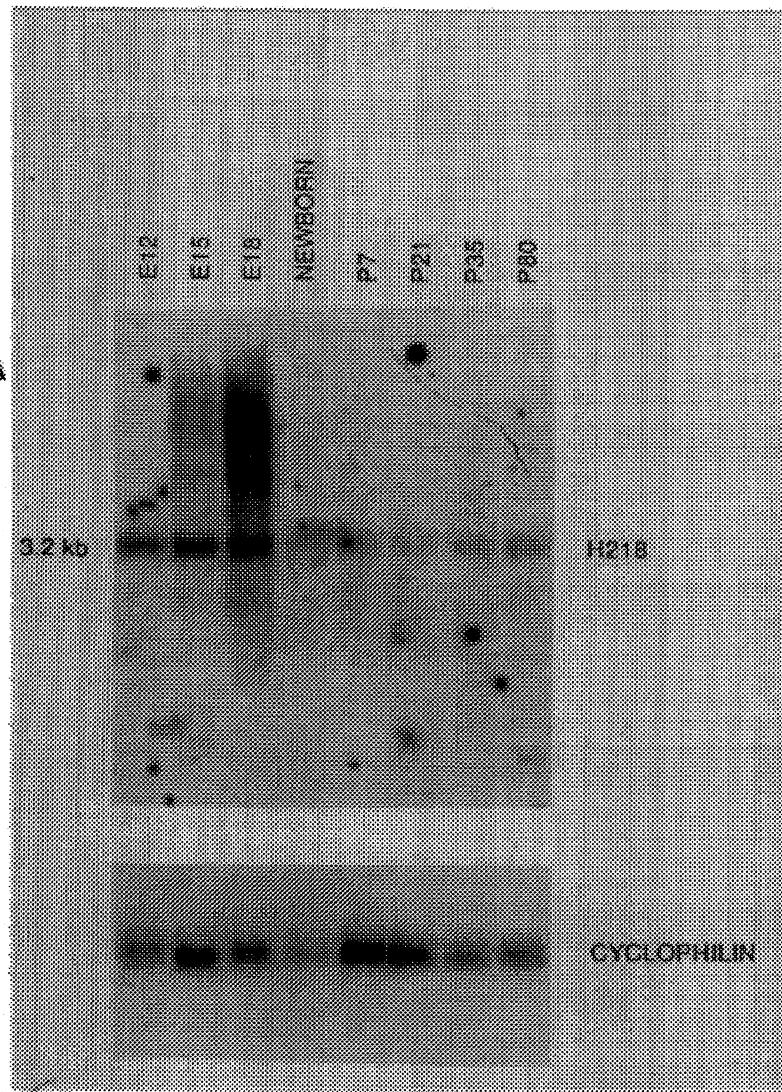
**U.S. Patent**

Jan. 5, 1999

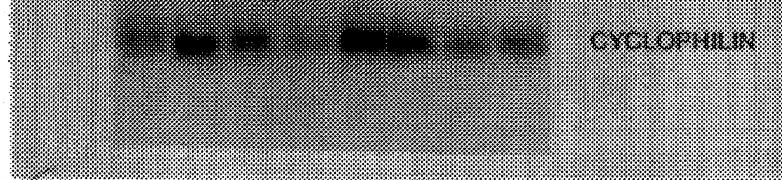
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**FIG. 3A**



**FIG. 3B**



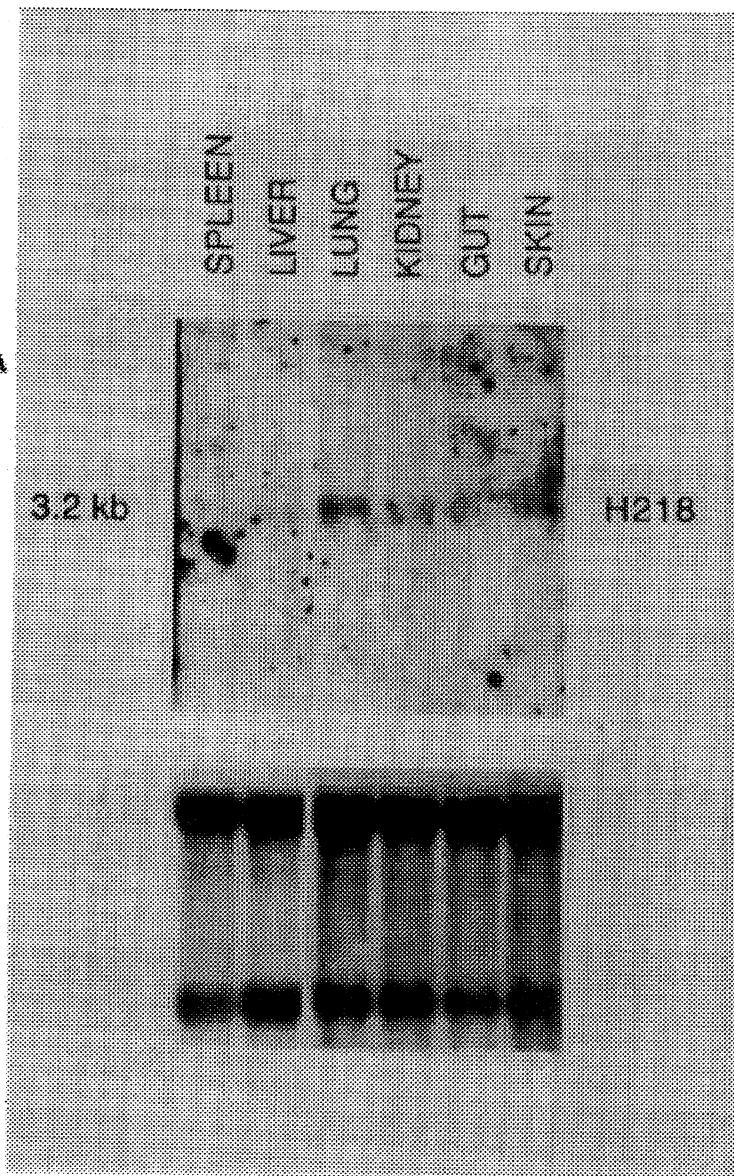
**U.S. Patent**

Jan. 5, 1999

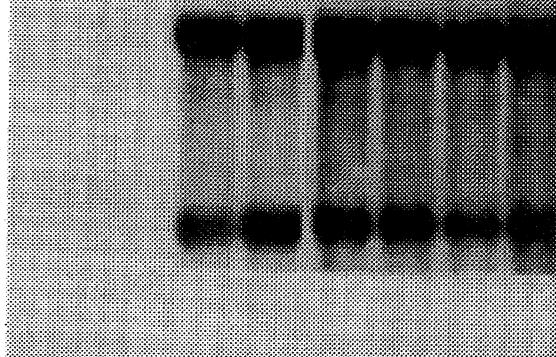
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**FIG. 4A**



**FIG. 4B**



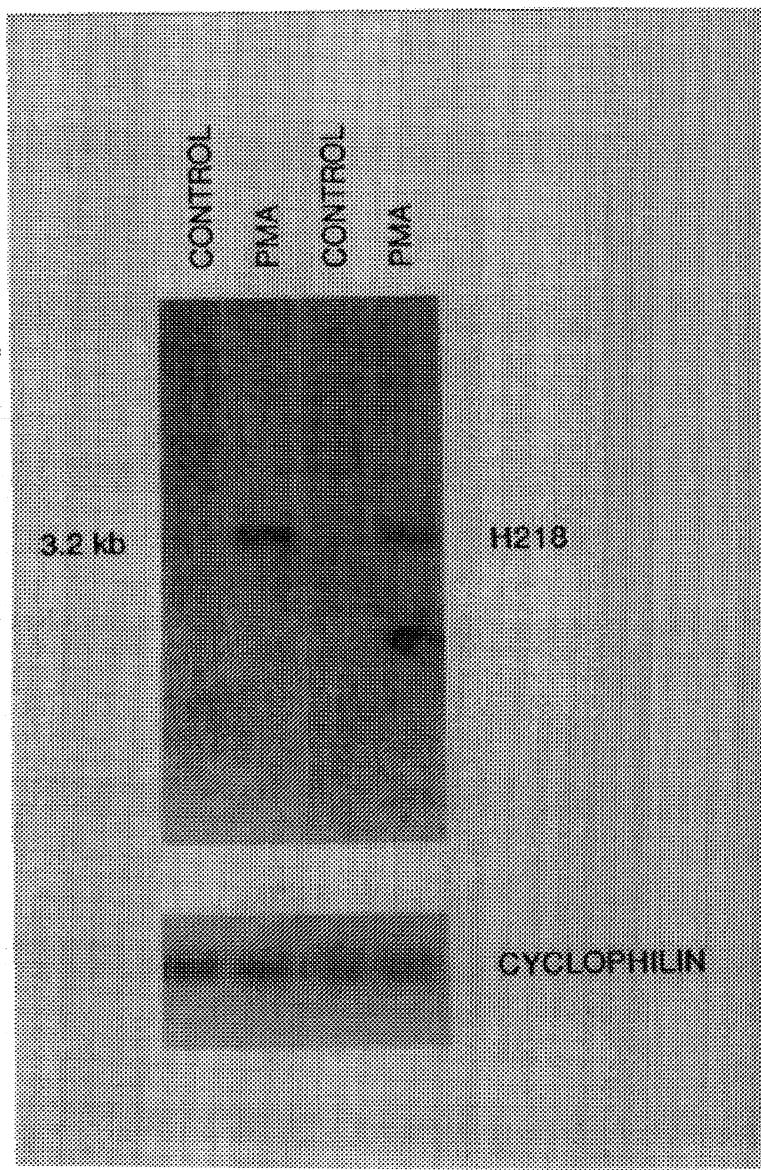
**U.S. Patent**

Jan. 5, 1999

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**FIG. 5A**



**FIG. 5B**

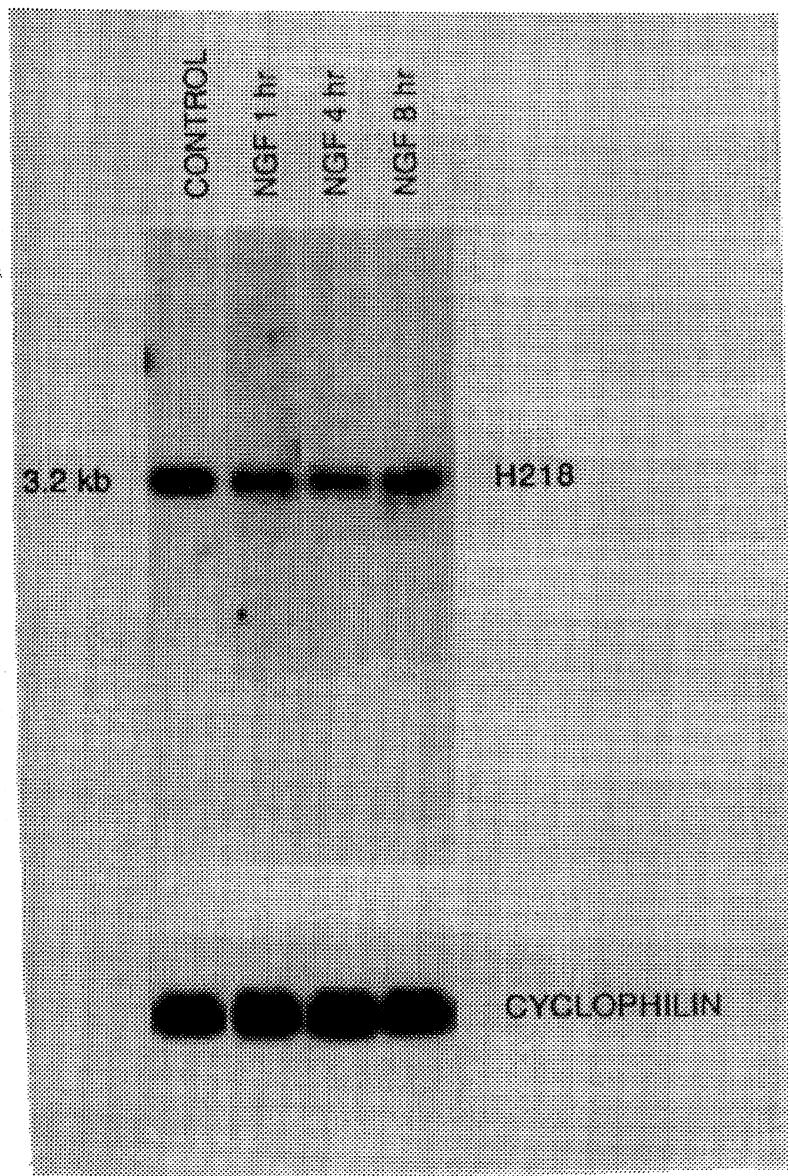
**U.S. Patent**

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**FIG. 6A**



**FIG. 6B**

CYCLOPHILIN